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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,449	01/09/2006	Bernd Schwenzer	101215-189	1690

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,449	SCHWENZER ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2008 and 12 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,8,10,11,13-16,19-21,23-28 and 30* is/are pending in the application.

4a) Of the above claim(s) *13-16,19-21 and 23-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,8,10,11,28 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on April 3, 2008 and March 12, 2009.

Currently, claims 1-2, 4, 8, 10-11, 13-16, 19-21, 23-28, and 30 are pending in the instant application. Claims 13-16, 19-21, and 23-27 have been withdrawn as being drawn to non-elected inventions. Accordingly, claims 1-2, 4, 8, 10-11, 28, and 30 are under examination on the merits.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Response to Arguments

Applicant's arguments with respect to claims 1-2, 4, 8, 10-11, 28, and 30 have been considered but are moot in view of the claim amendments and new ground(s) of rejection. See below.

New Objections/Rejections Necessitated by Amendment

Claim Objections

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 2 depends from claim 1, which recites an antisense oligonucleotide selected from the group consisting of SEQ ID NO:10 and SEQ ID NO:13. However, the dependent claim, claim 2, recites that the antisense oligonucleotide "consists of SEQ ID NO:10 and SEQ ID NO:13", thereby claiming a polynucleotide consisting of two independent antisense oligonucleotides. As such, the subject matter of claim 2 does not further limit the single polynucleotide claimed in claim 1. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 28, and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is currently amended to recite a single antisense polynucleotide consisting of two distinct, separate polynucleotide sequences: SEQ ID NO:10 and SEQ ID NO:13. Hence, the claimed structure of the polynucleotide is internally inconsistent, thereby rendering the claim

indefinite. For examination purpose, the polynucleotide of claim 2 will be interpreted to mean a polynucleotide consisting of SEQ ID NO:10 or a polynucleotide consisting of SEQ ID NO:13.

Claim 28 recites "the target sequence consisting of region 2206-2225 (SEQ ID NO:4)" in lines 3-4 and "the target sequence region consisting of SEQ ID NO:10" in lines 5-6. As such, the claim recites two distinct target sequences: SEQ ID NO:4 and SEQ ID NO:10. However, it is found that SEQ ID NO:10 is not a target sequence (e.g., sense mRNA sequence), but a complementary (e.g., antisense) sequence to SEQ ID NO:4. Hence, the ambiguous claim language as currently amended renders the structure of the claimed polynucleotide indefinite. For examination purpose, the polynucleotide of claim 28 will be interpreted to mean a polynucleotide targeted to SEQ ID NO:4.

Claim 30 recites "the target sequence consisting of region 2331-2350 (SEQ ID NO:8)" in lines 3-4 and "the target sequence region consisting of SEQ ID NO:13" in lines 5-6. As such, the claim recites two distinct target sequences: SEQ ID NO:8 and SEQ ID NO:13. However, it is found that SEQ ID NO:13 is not a target sequence (e.g., sense mRNA sequence), but a complementary (e.g., antisense) sequence to SEQ ID NO:8. Hence, the ambiguous claim language as currently amended renders the structure of the claimed polynucleotide indefinite. For examination purpose, the polynucleotide of claim 28 will be interpreted to mean a polynucleotide targeted to SEQ ID NO:8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 4, 8, 10-11, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cech et al. (US 6,093,809, citation of record) in view of Ho et al. (*Nature Biotechnology,* 1998, 16:59-63) and Scherr et al. (*Nucleic Acids Research,* 2000, 28:2455-2461, applicant's citation).

The claims are drawn to a 20-mer antisense oligonucleotide of SEQ ID NO:10, which is complementary to SEQ ID NO:4, wherein the antisense oligonucleotide is modified by phosphorothioate bonds.

Cech et al. disclose a nucleotide sequence of SEQ ID NO:100 encoding human telomerase, wherein the nucleotide sequence of SEQ ID NO:100 comprises the instantly claimed target nucleotide sequence of SEQ ID NO:4 (see nucleotides 528-547 of SEQ ID NO:100). They teach that their invention includes "antisense molecules comprising the nucleic acid sequence complementary to at least a portion of the polynucleotide of SEQ ID NO:82, 100, and 173" further comprising "a pharmaceutically acceptable excipient and/or other compound". See

column 9, lines 31-38. They teach that antisense oligonucleotides further comprise chemical modifications such as phosphorothioate linkages for increased stability and half-life. See column 35. They teach that antisense molecules when used as probes are immobilized on a solid support such as porous gels used in Northern or Southern blot analysis. See columns 9, 16-17. Cech et al. do not teach a 20-mer antisense oligonucleotide complementary to nucleotides 528-547 of SEQ ID NO:100.

Ho et al. teach the state of antisense oligonucleotide design technology as of January, 1998. They teach that one can design 20-mer target-specific antisense oligonucleotides by experimentally identifying accessible mRNA target sites with oligonucleotide libraries (RNA mapping), followed by expression assays in cell culture with synthesized antisense oligonucleotides. They teach that "although RNA mapping may not identify every single accessible site, ODNs against every accessible site tested have been active (Table 1)." See page 61, left column. They also state the following: "the RNA mapping method consistently and reliably identifies multiple, active antisense sequences based on targeting accessible regions of the RNA…In all 8 regions, antisense ODNs reduced protein levels by at least 50% in cells. This result contrasts with "gene walking" methods in which only 25% to 35% of ODNs tested generally are active." See page 62, left column.

Scherr et al. teach an effective approach for successfully identifying antisense oligonucleotide (ODN) sequences by computational RNA accessibility prediction/ODN selection methods, which generate an "accessibility score" for each target site. They teach that the accessibility score is especially useful for selecting target sites for long target sequences that may

have a large number of target sites because the computer-generated accessibility score allows one to select the most favorable target sites. See the entire reference.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a phosphorothioate-modified, 20-mer antisense oligonucleotide targeted to SEQ ID NO:100 of Cech et al. by utilizing antisense oligonucleotide selection methods of Ho et al. or Scherr et al.

One of ordinary skill in the art would have been motivated to make an antisense oligonucleotide targeted to SEQ ID NO:100 of Cech et al., because Cech et al. expressly disclosed that making antisense molecules against SEQ ID NO:100 is within their invention. In making the antisense oligonucleotide as contemplated by Cech et al., one of ordinary skill in the art would have reasonably identified accessible sites of SEQ ID NO:100 of Cech et al. by utilizing antisense oligonucleotide selection methods of Ho et al. and/or Scherr et al., and thus would have reasonably obtained nucleotides 528-547 of SEQ ID NO:100 as one of the potential or favorable accessible sites for antisense inhibition, because both Ho et al. and Scherr et al. taught that their selection/screening methods are reliable and sufficient to enable one to successfully identify suitable target sites. Hence, one of ordinary skill in the art would have had a reasonable expectation of success in making a stable, phosphorothioate-containing antisense oligonucleotide that is complementary to nucleotides 528-547 of SEQ ID NO:100 of Cech et al. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Claims 1-2, 4, 8, 10-11, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuchiya et al. (US 6,608,188 B1 citation of record) in view of Ho et al. (*Nature Biotechnology,* 1998, 16:59-63) and Scherr et al. (*Nucleic Acids Research,* 2000, 28:2455-2461, applicant's citation).

The claims are drawn to a 20-mer antisense oligonucleotide of SEQ ID NO:10 complementary to SEQ ID NO:4 or SEQ ID NO:14 complementary to SEQ ID NO:8, wherein the antisense oligonucleotide is modified by phosphorothioate bonds.

Tsuchiya et al. teach a polynucleotide comprising an antisense strand of SEQ ID NO:1 or SEQ ID NO:9 or SEQ ID NO:11, whose nucleotides 621-640 correspond to the 20-mer sequence of SEQ ID NO:4 of the instant application and whose nucleotides 746-765 correspond to the 20-mer sequence of SEQ ID NO:8 of the instant application. They teach that the antisense polynucleotide inhibits human telomerase activity and can also be used as a probe kit that detects a cancer cell or as a therapeutic drug that treats cancer. See columns 3-4 and 9-11. They teach that the antisense polynucleotide comprises a phosphorothioate bond for increased nuclease resistance, cell permeability, and binding affinity. Tsuchiya et al. do not teach antisense oligonucleotides consisting of a 20-mer sequence targeted to nucleotides 621-640 or 746-765 of their SEQ ID NO:1 or SEQ ID NO:9 or SEQ ID NO:11.

Ho et al. teach the state of antisense oligonucleotide design technology as of January, 1998. They teach that one can design 20-mer target-specific antisense oligonucleotides by experimentally identifying accessible mRNA target sites with oligonucleotide libraries (RNA mapping), followed by expression assays in cell culture with synthesized antisense oligonucleotides. They teach that "although RNA mapping may not identify every single

accessible site, ODNs against every accessible site tested have been active (Table 1)." See page 61, left column. They also state the following: "the RNA mapping method consistently and reliably identifies multiple, active antisense sequences based on targeting accessible regions of the RNA…In all 8 regions, antisense ODNs reduced protein levels by at least 50% in cells. This result contrasts with "gene walking" methods in which only 25% to 35% of ODNs tested generally are active." See page 62, left column.

Scherr et al. teach an effective approach for successfully identifying antisense oligonucleotide (ODN) sequences by computational RNA accessibility prediction/ODN selection methods, which generate an "accessibility score" for each target site. They teach that the accessibility score is especially useful for selecting target sites for long target sequences that may have a large number of target sites because the computer-generated accessibility score allows one to select the most favorable target sites. See the entire reference.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a phosphorothioate-modified, 20-mer antisense oligonucleotide targeted to nucleotides 621-640 or 746-765 of their SEQ ID NO:1 or SEQ ID NO:9 or SEQ ID NO:11 of Tsuchiya et al. by utilizing antisense oligonucleotide selection methods of Ho et al. or Scherr et al.

One of ordinary skill in the art would have been motivated to make an antisense oligonucleotide targeted to nucleotides 621-640 or 746-765 of their SEQ ID NO:1 or SEQ ID NO:9 or SEQ ID NO:11 of Tsuchiya et al., because Tsuchiya et al. expressly disclosed that making antisense molecules against SEQ ID NO:1 or SEQ ID NO:9 or SEQ ID NO:11 is within their invention, wherein the antisense molecules inhibit human telomerase activity thereby useful

as a therapeutic agent or the antisense molecules detect cancer cells thereby useful as a probe kit. In making the antisense oligonucleotide as contemplated by Tsuchiya et al., one of ordinary skill in the art would have reasonably identified accessible sites of SEQ ID NO:1 or SEQ ID NO:9 or SEQ ID NO:11 of Tsuchiya et al. by utilizing antisense oligonucleotide selection methods of Ho et al. and/or Scherr et al., and thus would have reasonably obtained 20-mer nucleotide regions, nucleotides 621-640 and nucleotides746-765, as potential or favorable accessible sites for antisense inhibition, because both Ho et al. and Scherr et al. taught that their selection/screening methods are reliable and sufficient to enable one to successfully identify suitable target sites. Hence, one of ordinary skill in the art would have had a reasonable expectation of success in making a stable, phosphorothioate-containing antisense oligonucleotide that is complementary to nucleotides 621-640 and nucleotides746-765 of SEQ ID NO:1 or SEQ ID NO:9 or SEQ ID NO:11 of Tsuchiya et al. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Conclusion

No claim is allowed.

This application contains claims 13-16, 19-21, and 23-27 drawn to inventions nonelected with traverse in the reply filed on June 1, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner, Art Unit 1635